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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/837,562	04/19/2001	Edward Larry McCleary	12439.101B	7515

24283 7590 07/28/2003

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EXAMINER
MCINTOSH III, TRAVISS C

ART UNIT	PAPER NUMBER
1623	15

DATE MAILED: 07/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/837,562	MCCLEARY, EDWARD LARRY	
	Examiner	Art Unit	
	Traviss C McIntosh	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-64* is/are pending in the application.

4a) Of the above claim(s) *2-23 and 25-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,24 and 53-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Amendment filed May 14, 2003 has been received, entered into the record, and carefully considered. The following information provided in the amendment affects the instant application by:

Claims 2-23 and 25-52 have been withdrawn.

Claims 1 and 24 have been amended.

New claims 53-64 have been entered.

The title has been amended.

The specification has been amended on page 15, lines 16-18 and lines 23-24 as indicated.

Remarks drawn to rejections of Office Action mailed February 11, 2003 include those drawn to:

Specification objection: which has been withdrawn due to applicant's amendments.

112 1st paragraph rejections for lack of written description: which has been withdrawn as applicant's arguments were found to be convincing.

112 1st paragraph rejections for scope of enablement: which is maintained for reasons of record.

112 2nd paragraph rejections: some of which have been obviated by applicant's amendments. A further discussion is set forth below.

An action on the merits of claims 1, 24, and 53-64 is contained herein below. The text of those sections of Title 35, US Code which are not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 24 and 59-64 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The instant disclosure is not seen to be sufficient to enable the use of any compound which comprises active agents A-F, to normalize impaired or deteriorating neurological function without undue experimentation. This rejection is correlative to the rejection of claims 24, 27, 29, 33, 35, 36, and 46-52 of the previous office action.

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in ***In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)***. A conclusion of lack of enablement means that, based on the evidence regarding a fair evaluation of an appropriate combination of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. It is noted that ***In re Wands*** is cited to show the factors which are relied upon to determine if an application is enabled for what is claimed, not to show what courts decided in respect to the position of the examiner, therefor applicant's arguments which compare the instant application to Wands are moot.

These factors include:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims – The nature of the invention

Claim 24 is drawn to a method for treating impaired neurological function or treating deteriorating neurological function in a human comprising administering a composition comprising:

(A) an agent which promotes ATP and or creatine phosphate synthesis;

(B) an antioxidant for scavenging free radicals in at least one pathway in the body;

(C) an agent for normalizing or maintaining membrane function and structure;

(D) an agent for normalizing or maintaining normal neurotransmitter function;

(E) an agent for down-regulating cortisol action; and

(F) an agent for suppressing activation of apoptotic pathways.

Dependent claims 59-64 limit the active agents wherein (A) is B-vitamins, (B) is ALA, (C) is a methyl-donor, (D) is huperzine A, (E) is pyridoxine, and (F) is vinpocetine respectively. It is noted that the claims read on treating and curing any and all diseases relating to the nervous system and neurological disorders, including curing paralysis, multiple sclerosis, and Alzheimer's Disease as applicants define impaired neurological function as deteriorating or defective neurological function on page 17, lines 25-26 of the specification, and on page 18, the last sentence of the first full paragraph of the response submitted May 14, 2003 applicants state, "any detectable degree of deterioration falls within the scope of the patent".

The state of the prior art

Neurological disorders and nervous system diseases are known to be localized in the following sites: muscle, motor end plate, peripheral nerves, spinal nerve roots, spinal cord, brainstem, cerebellum, basal ganglia and thalamus, and cerebral hemispheres. Pathologies include genetic disease, infections, trauma, neoplasms, metabolic disorders, toxic disorders, endocrine disorders, vascular diseases, demyelinating and degenerative disease, electrical disorders, and autoimmune disorders. Nervous system and neurological diseases can belong to the following classes: the peripheral system diseases, disease of the neuromuscular junction, diseases of muscle, the spinal cord, cranial nerves, the cerebellum, the basal ganglia, the cerebrum, unlocalized or multifocal disorders, and demyelinating diseases. Heavy metals (e.g., arsenic, lead, thallium, gold, manganese, and mercury), synthetic chemicals (e.g., organophosphates, gasoline, and toluene), alcohols (especially ethyl and methyl alcohol), ionizing radiation, and many drugs can all be toxic to the nervous system. In addition, water overload can cause seizures, and oxygen, under high pressure, can induce depression of brain function. Many drugs and other agents are capable of causing damage to cranial nerves or peripheral nerves. There are compounds which are known to have beneficial effects on certain nervous system disorders, for example, human phosphoprotein polypeptide (hPSHP) - useful for treating degenerative neuronal diseases e.g. Parkinson's and Huntington's disease (Hillman et al. 5,971,028), but none are known to cure all nervous system disorders.

Pyridoxine (vitamin B_6) is a well-known vitamin normally used as an adjunct in prophylaxis and treatment of multiple vitamin B complex deficiencies. It is also used in dermatoses, neuromuscular and neurological diseases as seen in Coffen et al. (Us Patent 4,026,901).

Lipoic acid prevents free radical damage to cells and cell components and has been shown to maintain microsomal protein thiols, protect against hemolysis, and protect against neurological disorders as seen in Perricone et al. (US Patent 5,709,868).

Compositions comprising methyl donors, particularly methylcobalamin, provide a method for treating a host with neurological dysfunction associated with an immunological disorder. The methyl donor compounds are also used to restore normal metabolic biochemical functions after immune mediated disruption of biochemical pathways as seen in Rabinoff et al. (US patent 5,508,271).

Acetylcholinesterase inhibitors (e.g., huperzine A and B) provide relief of symptoms of apathy, delusions, hallucinations and irritability in Alzheimer's disease patients as seen in Kaminski et al. (US Patent 5,889,033).

Vinpocetine possesses antioxidant activity which exerts significant protective action in events of cerebral ischemia (transient ischemic attack (TIA), stroke), where the injury of learning and memory may occur in addition to neurological symptoms of various severity as seen in Szantay et al. (US Patent 6,093,720).

As with all compositions containing multiple active agents, one would appreciate that the parameters surrounding each compound used in a combination for use in treatment will vary depending on a multitude of conditions, including the disease treated, the particular compounds used, the route of administration, and the condition and age of the patient. Additionally, one would recognize the possibilities of compounds having either synergistic or deleterious effects upon each other due to the reactions they can undergo with each other.

It is noted that applicants acknowledge in their response and have submitted references in a supplemental IDS that each of the functions are well-known in the prior art.

The level of one of ordinary skill

The skilled artisan in this field is that of an MD for neurological disorders and/or a PhD skilled in the development of therapeutics for neurological disorders.

The level of predictability in the art

The examiner acknowledges the probability and predictability that the active agents independently selected, indeed have efficacy in treating certain specific symptoms associated with certain specific neurological disorders, however the art appears to be silent with regard to the predictability of effectively treating and curing all neurological disorders by administering any of the indicated compounds, or in their combination. One skilled in the art would not predict from the disclosure that all neurological disorders or symptoms could be effectively treated and cured by administering the composition of the instant application.

Applicants argue that a requirement of patentability is not that the claimed compound must show efficacy in treating all neurological disorders, and that the showing in the specification of the compound treating six disorders is well recognized in the law as an adequate basis for the claim. The examiner requests applicants to provide guidance as to where such case law exists, that is, where is there case law showing that generalized statements in the specification in regards to various disorders is adequate guidance as to a compound treating any and all neurological disorders? Applicants appear to be arguing limitations which are not in the claims, the claims read "a method for treating impaired neurological function or treating

deteriorating neurological function in a human...". As set forth supra, applicants even state "any detectable degree of deterioration falls within the scope of the patent".

The amount of direction provided by the inventor

The instant specification is not seen to provide adequate guidance which would allow the skilled artisan to extrapolate from the disclosure and examples provided to use the claimed method commensurate within the scope of the claims. There are no control groups where a skilled artisan could conclusively state that the positive effects are tied to the administration of the combined compounds. There is no data which adequately represent the complete scope of the claims as written. Further, there is no evidence in the disclosure that the composition as claimed would have any beneficial effect on a human patient. Although the instant specification provides guidance on various pathways involved in neurological activity, it is not seen to provide guidance for the use of the composition as claimed to effectively act in the manner claimed.

Applicants argue that one skilled in the art can make more than a hundred examples of the claimed invention. The examiner acknowledges that one skilled in the art could combine different agents listed and form various compositions, as that requires generalized formulation techniques, but one skilled in the art would not come to the conclusion that the compositions indeed have efficacy in treating any and all neurological disorders.

The existence of working examples

There are no working examples set forth in the instant specification.

Applicants state there are working examples given for each of the agents and for preferred combinations of agents. The examiner acknowledges that there is generalized

information on the activity of the various agents, but there is nothing in the specification showing a specific composition and it's use in the treatment of any disease.

The quantity of experimentation needed to make and use the invention based on the content of the disclosure

Indeed, in view of the information set forth supra, the instant disclosure is not seen to be sufficient to enable the use of the composition as claimed, to treat and/or cure any/all neurological disorders or symptoms without undue experimentation. One skilled in the art could not use the claimed invention without undue experimentation.

Claims 1, 24, and 53-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "normalizing" and in claims 1 and 24 is a relative term which renders the claims indefinite. The term "normalizing" is not defined by the claims, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. What level is meant to be normal, and what level is not intended as normal? Clarity is respectfully requested. It is noted that applicants replaced "normalizing" with "treating" in the preamble of claims 1 and 24, but agents represented by (C) and (D) still have this recitation.

Claims 56 and 62 are indefinite as applicants have defined component (D) as hyperzine, yet applicants have not disclosed this compound before. The examiner believes applicants intended to recite huperzine A. It is noted that if applicants intended hyperzine, the examiner

requires applicants point out to where this recitation would have proper antecedent support in the case and would therefor not be new matter.

Claims 59-64 are indefinite. The claims are all dependent upon claim 24 which is drawn to a method of treatment comprising administering a composition. Claims 59-64 are all drawn to "a composition according to claim 24...". These claims would be more favorably written as "a method of claim 24 wherein component (X) of the composition comprises..." as this would properly relate the independent method claim to the dependent method claims.

Conclusion

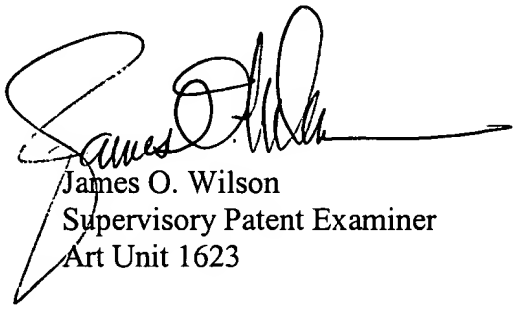
Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C McIntosh whose telephone number is 703-308-9479. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 703-308-4624. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



James O. Wilson
Supervisory Patent Examiner
Art Unit 1623

Traviss C. McIntosh III
July 25, 2003